

heating bath, the proportions of the reactants and the length of the reaction period were varied as shown in Table I.

Summary

1. A compound which appears to be a complex of one molecule of α -hydroxy- α -acetamino-propionic acid and two molecules of acetamide has been isolated as a by-product of the condensation of pyruvic acid and acetamide.

2. A method of preparing the complex in good yield from pyruvic acid and acetamide is described; it indicates that the complex probably represents the first step in the condensation reaction.

3. Attempts to modify the conditions of the condensation of pyruvic acid and acetamide in such a way as to make α -acetaminoacrylic acid the principal product were not successful.

NEW YORK, N. Y.

RECEIVED NOVEMBER 10, 1938

[CONTRIBUTION FROM THE BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, U. S. DEPARTMENT OF AGRICULTURE]

Crystalline Solvates of Inactive Deguelin

BY LYLE D. GOODHUE AND H. L. HALLER

Extractives prepared from derris and cube contain, besides rotenone, principally deguelin. Certain types of derris also contain considerable amounts of toxicarol and some sumatrol.¹ Deguelin and tephrosin have never been obtained by direct crystallization, but are only obtained in the inactive form² when the extractives are treated with mild alkali.

Rotenone crystallizes from certain organic liquids with a definite molecular ratio of rotenone to solvent of crystallization. A number of these solvates have been investigated,^{3,4} primarily because of their possible use in methods for the determination of rotenone. The solvates formed with carbon tetrachloride and dichloroacetic acid have been shown to be of value in the analysis of derris and other rotenone-bearing plants, and under the conditions employed rotenone is the only compound that separates when extractives of these plants are treated with these solvents. Deguelin probably occurs in the plant in the levo form,⁵ and solvates, if formed during the determination of rotenone, are either too soluble or their melting points too low for ready crystallization.

It has now been found that racemic deguelin forms definite stable solvates with a number of solvents, and several of these are reported in this paper.

After it was observed that inactive deguelin

separated from chloroform as the solvate, all the readily available solvents were examined for solvate formation with this compound. It was found that carbon tetrachloride, chloroform, bromoform, and ethylene bromide form definite stable solvates in a ratio of 1 mole of deguelin to 1 of solvent. Although no definite data have yet been obtained, it is evident that the carbon tetrachloride solvate is the least soluble and, just as in the determination of rotenone, it would be the most suitable for deguelin. The solvate with bromoform would be excellent because of its high molecular weight, but it is too soluble to crystallize without the addition of petroleum ether.

In a comparison of the liquids that form solvates with rotenone and deguelin it is interesting to note that, so far as is shown, only carbon tetrachloride and chloroform are capable of forming solvates with both these closely related compounds. Rotenone forms solvates with many organic acids and benzene, but not with bromobenzene, chlorobenzene, or ethylene bromide, whereas deguelin forms solvates with the last three and not with organic acids or benzene. Neither rotenone nor deguelin was found to form solvates with aliphatic hydrocarbons, alcohols, ketones, and ethers. Little is known about solvate formation but with the rotenone group of compounds it appears that solvate formation is more likely to occur when the solvent molecule possesses a negative substituent. Not all compounds containing such a substituent, however, form solvates. This generalization is a useful working tool in the search for new solvates.

The methods for the determination of rotenone depend upon the formation of a sparingly soluble

(1) Cahn and Boam, *J. Soc. Chem. Ind.*, **54**, 42T (1935).

(2) Clark, *THIS JOURNAL*, **53**, 313 (1931).

(3) Tattersfield and Roach, *Ann. Appl. Biol.*, **10**, 1 (1923); Jones and Smith, *THIS JOURNAL*, **52**, 2554 (1930); Jones, *ibid.*, **53**, 2738 (1931); Jones, U. S. Patent 1,942,104 (Jan. 2, 1934).

(4) Jones, U. S. Patent 2,103,195 (Dec. 21, 1937); Jones, *Ind. Eng. Chem., Anal. Ed.*, **10**, 684 (1938).

(5) Haller and LaForge, *THIS JOURNAL*, **56**, 2415 (1934).

solvate with carbon tetrachloride. A similar method might be developed for deguelin. After the rotenone has been removed, the resin which remains could be treated with mild alkali and the separated racemic deguelin determined in the form of a solvate. The details of such a procedure will be described in a later paper.

Experimental

Preparation of Inactive Deguelin.—The deguelin used in these studies was prepared from cube root by a modification of the method used by Clark.² Since the procedure differs in several details, it will be described briefly.

About 5 kg. of finely ground cube root was percolated for two days with 18 liters of chloroform. The chloroform was removed under reduced pressure, and the resin was taken up in 2 volumes of carbon tetrachloride, from which the rotenone was allowed to crystallize as the solvate. After removal of the rotenone, the resin was freed of fats and waxes by adding, with stirring, petroleum ether until no more resin was precipitated. The petroleum ether-soluble material was discarded. The resin was taken up in ether and extracted five times with 5% alkali in saturated sodium chloride. At this point a large part of the color was removed with the phenolic substances. The extraction was carried out in the shortest possible time, and the ether solution was washed immediately with dilute acetic acid to prevent the oxidation of deguelin to tephrosin which takes place in the presence of alkali. The ether was removed, leaving 150 g. of purified extractives. For racemization this material was dissolved in 2 liters of hot methanol in a 5-liter round-bottomed flask. Atmospheric oxygen was removed by evacuation, and 20 cc. of 10% potassium hydroxide was added through a dropping funnel.

After twenty-four hours the crystalline material that separated (60 g.) was crystallized from chloroform five times as the solvate and twice from alcohol. This procedure gave 25 g. of pure white deguelin melting at 167° (corr.). The optical properties checked with those of a known sample of deguelin, and the red color⁶ was 81% of that given by pure rotenone, which agrees with that obtained by Cahn, Phipers, and Boam.⁷ The sample was inactive to polarized light.

Tests for Solvate Formation.—To determine whether deguelin forms a solvate, 0.5 g. was dissolved in 2 cc. of warm solvent and cooled in ice water. With those solvents that form solvates it was necessary to start crystallization by scratching or by evaporating some of the solution on a stirring rod. The crystals were collected on a weighed Gooch containing a small disk of filter paper. The uncombined solvent was removed by drawing air through the crystals until the weight was constant. The solvent of crystallization was then determined as loss of weight at 110° under a pressure of 25 mm. Even the higher boiling solvents were completely removed in one hour by this procedure.

The bromoform solvate is too soluble to crystallize from bromoform without the addition of an equal volume of

petroleum ether. In the preparation of the carbon tetrachloride solvate 0.5 g. will not dissolve in 2 cc.; so 4 cc. was taken and the solution was reduced to 2 cc. This is true of some of the solvents that did not form solvates. In the case of benzaldehyde it was necessary to dry by drawing air through the crucible overnight.

The solvents tested by this method, that formed solvates, are listed in Table I. Those that crystallized with deguelin in the ratio of 1 mole of deguelin to 1 mole of solvent were bromoform, carbon tetrachloride, chloroform, and ethylene bromide, all of aliphatic origin. Those that crystallized with 2 moles of deguelin to 1 of solvent were aromatic compounds, namely, bromobenzene, chlorobenzene, and benzaldehyde. None of the solvates showed a detectable loss of solvent in twenty-four hours. The chloroform solvate after two weeks in air contained 22.2% of chloroform as compared with 23.2% for the theoretical. The carbon tetrachloride solvate if heated slowly loses its solvent of crystallization and melts at 167°, the same as deguelin. The chloroform solvate behaves in like manner, but the solvate with ethylene bromide melts at 130–135° and remains liquid. The melting points of the others were not taken.

TABLE I
TESTS WITH DIFFERENT SOLVENTS FOR SOLVATE FORMATION WITH DEGUELIN

Solvent	Crystals dried at room temp., g.	Loss at 110° and 25 mm., g.	Loss, %	Theoretical loss, %
Solvate formed in 1:1 ratio of deguelin to solvent				
Bromoform	0.5573	0.2188	39.2	39.1
	.1233	.0473	38.5	
Carbon tetrachloride	.7227	.2005	27.7	28.1
	.7447	.2197	29.5	
Chloroform	.3041	.0719	23.6	23.2
	.3383	.749	22.1 ^a	
Ethylene bromide	.3704	.1154	31.1	32.4
	.2338	.0735	31.4	
Solvate formed in 2:1 ratio of deguelin to solvent				
Benzaldehyde	0.3377	0.0434	12.8	11.1
	.3283	.0443	13.5	
Bromobenzene	.4398	.0745	16.9	16.6
	.4027	.0687	17.0	
Chlorobenzene	.4291	.0551	12.8	12.5
	.4109	.0529	12.9	

^a Loss from solvate prepared two weeks earlier.

It was found that deguelin crystallized unsolvated from the following solvents: acetic acid, benzene, *n*-butyl alcohol, *s*-butyl bromide, dichloroethylene, α,α' -dichlorodiethyl ether, dioxane, ethylene chloride, ethylene chlorohydrin, methyl ethyl ketone, methyl iodide, nitromethane, and propylene bromide.

Attempts were also made to form solvates with halogen-substituted organic acids. Because of their low volatility the above procedure could not be used. Deguelin was dissolved in the warm acid and crystallization was induced by slowly diluting with water. The crystals were washed free of acid and titrated in a flask containing chloroform and water. Solvates of rotenone with organic acids

(6) Goodhue, *J. Off. Agr. Chem.*, **19**, 118 (1936).

(7) Cahn, Phipers and Boam, *J. Chem. Soc.*, 513 (1938).

can be prepared and determined in this way,⁴ but deguelin either does not form solvates or they are decomposed by water. The acids tried were dichloroacetic, α -bromopropionic, α -chloropropionic, α -bromobutyric, and lactic. Crystallization induced with petroleum ether instead of water also gave no solvate.

Summary

Seven stable solvates of inactive deguelin are

reported. Deguelin crystallizes from carbon tetrachloride, chloroform, bromoform, and ethylene bromide with 1 mole of solvent to 1 mole of deguelin, and from bromobenzene, chlorobenzene, and benzaldehyde with 1 mole of solvent to 2 moles of deguelin.

WASHINGTON, D. C.

RECEIVED DECEMBER 15, 1938

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

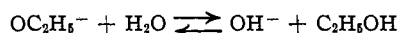
Kinetics of the Reactions of Ethyl Iodide with Bases in Ethyl Alcohol-Water Mixtures¹

BY SAM EAGLE AND J. C. WARNER

In beginning an investigation of the reactions of alkyl halides which occur in solution, we have made an extensive study of the reactions of ethyl iodide with sodium hydroxide, triethylamine, sodium acetate and with the solvent in ethyl alcohol and aqueous alcohol mixtures at 50 and 25°. Sufficient experiments have been carried out with lithium nitrate to establish the importance of the role of nitrate ion as a primary reactant exclusive of the "inert salt catalysis." The over-all rate has been corrected successfully for side reaction of the halide with the solvent and the rate of reaction with various bases has been correlated with their base strength. The effect of changing medium has been partially assigned to the influence of dielectric constant on the base strength. Approximate values of the energies of activation at constant composition and constant dielectric constant have been obtained for the various reactions. Considerable progress has been made toward an explanation of the "dilution effect" without the assumption of reaction of ethyl iodide with molecules of strong electrolytes.

Many kinetic studies on the reactions of ethyl iodide and other alkyl halides have been reported in the literature. The results of these previous investigations may be summarized briefly as follows. In the reactions of sodium ethylate and ethyl iodide in ethyl alcohol, the bimolecular constants show a pronounced "dilution effect," the value of the constant decreases with increased base concentration,² but is independent of the halide concentration. The reported temperature coefficient is 20,650 cal. The velocity constant

decreases in aqueous alcohol solutions with addition of water, and the existence of an equilibrium



is well established.^{3a} The rate increases with pressure.^{3b} The calculated constants for many of the reactions of this type show a downward drift with time which is traceable to loss of halide, side reactions, or to the magnifying of errors when using the analytical method for obtaining velocity constants.

Menschutkin⁴ measured the velocity of formation of tetraethylammonium iodide in a number of solvents and found a pronounced dependence of the rate on the medium in which the chemical change was produced. Many attempts to correlate the measured velocity constants with various properties of the solvent have been made,⁵⁻⁷ but the specific influence of the medium has been poorly understood. The energies of activation for the amine-halide reactions vary markedly with the solvent and generally fall below the normal range of around 20,000 cal., commonly found for bimolecular reactions in solution.⁸ That a part of the conversion of ethyl iodide to inorganic iodide arises from reaction with the solvent has frequently been suggested, but a thorough investigation of this side reaction has not been reported. The recent work of Taylor⁹ and Hughes and Shapiro¹⁰ on the alcoholysis of ethyl and hy-

(3) (a) De Bruyn and Steger, *Rec. trav. chim.*, **18**, 311 (1899); (b) Gibson, Fawcett and Perrin, *Proc. Roy. Soc. (London)*, **A150**, 233 (1935).

(4) Menschutkin, *Z. physik. Chem.*, **6**, 41 (1890).

(5) Grimm, Ruf and Wolff, *Z. physik. Chem.*, **B13**, 301 (1931).

(6) Soper and Williams, *J. Chem. Soc.*, 2297 (1931).

(7) Walden, *Chem. Z.*, **81**, 904 (1907).

(8) Moelwyn-Hughes, *Chem. Rev.*, **10**, 241 (1932).

(9) Taylor, *J. Chem. Soc.*, 992 (1937).

(10) Hughes and Shapiro, *ibid.*, 1177 (1937).

(1) Abstracted from a thesis submitted by Sam Eagle to the Committee on Graduate Instruction in partial fulfillment of the requirements for the degree of Doctor of Science.

(2) Hecht, Conrad and Brückner, *Z. physik. Chem.*, **4**, 273 (1889); **5**, 589 (1890).